## REMARKS/ARGUMENTS

Claims 1-20 are pending. Claims 1-9 are rejected. Claims 10-20 are withdrawn due to restriction requirement.

Support for amendment of claim 1 can be found at p.2, lines 16-26, in original claim 3 (which has been canceled), and in the paragraph spanning pages 26-27. Claim 1 has been amended to recite nucleotides 36-1171 of SEQ ID NO:1. The first 35 nucleotides of SEQ ID NO:1 correspond to primer and adaptor sequences used in the isolation of SEQ ID NO:1.

The paragraph spanning pages 26-27 of the specification explains that the gene 513 fragment was amplified using a Marathon cDNA Amplification kit from Clontech, and that the amplification was carried out using the adaptor primer supplied with the kit and a primer specific to gene 513 (SEQ ID NO:9). The paragraph also explains that the "nucleotide sequence of the fragment was found to be 1171 bp ... This sequence is shown as SEQ ID NO:1."

Attached is a page from the Clontech Marathon cDNA Amplification Kit User Manual. The page shows the sequence of the 23 nucleotide AP2 adaptor primer and additional adaptor sequence that corresponds to nucleotides 24-35 of SEQ ID NO:1. The "Marathon cDNA Adaptor", as described in the Marathon protocol, is ligated to the ends of double stranded cDNA isolated from a cell. The cDNA is then amplified using an Adaptor Primer and a primer that is specific to the gene to be amplified, as described in the paragraph spanning pages 26-27 of the specification. One skilled in the art, having read this section of the specification, would expect the Marathon cDNA Adaptor sequence to constitute the end of SEQ ID NO:1. This expectation would be met by the fact that the end of SEQ ID NO:1 does constitute the Marathon cDNA Adaptor sequence. The amendment of claim 1 (and claims 4-6) to recite nucleotides 36-1171 of SEQ ID NO:1 adds no new matter because one skilled in the art would reasonably understand from the specification that applicants had possession of nucleotides 36-1171 of SEQ ID NO:1 as the actual sequence of gene 513, separate from nucleotides 1-35 which are derived from the adaptor sequence used to amplify the fragment.

Support for amendment of claim 4 can be found in the paragraph spanning pages 26-27, p.23, lines 1-23, and p. 24, lines 22-28. Support for amendment of claim 5 can be found in

original claim 9 (which has been canceled), original claim 3 (which has been canceled), p.25, lines 13-20, p.11, lines 10-17, and the paragraph spanning pages 26-27. Support for amendment of claim 6 can be found in original claim 9 (which has been canceled), p.23, lines 1-23, p.25, lines 13-20, p.11, lines 10-17, and the paragraph spanning pages 26-27.

**Claim Objections**

The Examiner says that claim 3 is broader in scope than claim 1, and therefore is an improper dependent claim. The Examiner says that claims 4-9 depend from claim 1 but do not include all the limitations of claim 1.

Claim 3 has been canceled. Claims 4, 5 and 6 have been amended to refer to specific nucleotide sequences rather than claims 1-3. Claims 4, 5 and 6 as amended do not depend from claims 1 or 3.

**35 U.S.C. § 112, First Paragraph**

The Examiner has rejected claims 1-9 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time the application was filed. Specifically, the Examiner has rejected composition of matter claim 1 for reciting the word "comprising" when SEQ ID NO:1 is a partial cDNA. Claim 1 has been amended by replacement of the word "comprising" with the words "consisting of". Claims 2 and 3 have been canceled.

The Examiner has rejected method claims 4-9 under the same rationale. Specifically, the Examiner says that the large genus of nucleic acids encompassed by claims 4-9 is represented by a nucleic acid consisting of instant SEQ ID NO:1. The Examiner further says that the applicant has express possession of only one species in a genus which comprises many, many different possibilities.

The issue of written description "most typically...arise[s] in the context of determining whether new or amended claims are supported by the description of the invention in the application as filed, whether a claimed invention is entitled to the benefit of an earlier priority date or effective filing date under 35 U.S.C. §119, 120 or 365(c), or whether a specification

provides support for a claim corresponding to a count in an interference." MPEP § 2163 at p.2100-160, col. 1, 2nd paragraph (citations omitted). In other words, the main context in which the written description requirement arises is a situation in which there is an issue related to new matter. Although independent claims 4-6 have been amended, the amendments are fully supported by the specification and do not add any information that constitutes new matter. There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. MPEP § 2163 at p.2100-160, col. 2, 2nd paragraph. Because new matter is not an issue, claims 4-9 are entitled to the presumption that they are adequately described.

The Vas-Cath case cited by the Examiner arose in the typical context of determining new matter (Vas-Cath v Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991)). Specifically, the issue was whether drawings of a catheter in a design application provided written description of claims that appeared in a utility application claiming priority to the design application. Vas-Cath addresses new matter and does not address what written description is required for originally filed claims. As stated above, new matter is not an issue with respect to the present claims.

Despite the strong presumption that an adequate written description of the claimed invention is present when the application is filed, this presumption may be overcome when the claims require an essential feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill (see MPEP § 2163 pp.2100-160, 2nd col., 1st paragraph). Most, if not all of the Federal Circuit decisions addressing written description when new matter is not an issue do so in the context of de novo isolation of nucleic acids. Thus, the Examiner cites Fiers v Revel for the proposition that "if an inventor is unable to envision the detailed chemical structure of DNA sequence coding for specific protein, as well as a method of obtaining it, then conception is not achieved..." 25 USPQ2d 1601, 1604 (Fed. Cir. 1993). Fiers is not applicable to the present facts and circumstances because Fiers involved a situation in which no nucleic acid sequence was disclosed. Fiers was based on an interference proceeding, in which both parties claimed the same gene sequence. In the quest for an early conception date, Fiers attempted to establish a date of conception for a complete cDNA before he had any nucleotide sequence. In the instant

case, applicants have a nucleotide sequence. The nucleotide sequence of nucleotides 36-1171 of SEQ ID NO:1 is sufficient to distinguish claims 4-9 from the prior art. Thus, unlike in Fiers, applicants have described the claimed subject matter by a structural feature that distinguishes the claims from the prior art. Such meets the standard of University of California v. Eli Lilly, 43 USPQ2d 1398 (Fed. Cir 1997).

It is acknowledged that the Examiner Written Description Guidelines Training Materials provide an example of an applicant disclosing an EST and attempting to claim a nucleic acid comprising the EST (example 7 of the Training Materials). The Training Materials indicate that such a claim violates the written description requirement because the disclosed structural feature of the EST does not constitute the principal attribute of a cDNA, namely the coding sequence. The Training Materials do not of course have the force and effect of law, and it remains to be determined whether this position will be supported by the Federal Circuit. In any event, the Training Materials do not address the situation in which applicants claim a hybridization detection *method* using a nucleic acid comprising a partial gene sequence. Irrespective of whether the Training Materials are correct in their position with respect to a composition claim, it is respectfully submitted that such a method claim meets the test of written description.

The analysis for a method claim differs from a composition claim because additional sequences flanking a disclosed partial sequence are not essential to practice of a hybridization method, whereas such flanking sequences are essential to what is usually the most important attribute of a gene, namely the capacity to express a fully functional protein. For composition of matter claims that recite "comprising" a gene sequence, the complete gene sequence can be viewed as an essential part of the claims. The complete gene sequence is essential because it is usually not possible to express a gene to obtain a fully functional protein unless the complete cDNA sequence is known. By contrast, the complete sequence of a cDNA is not essential for a method of DNA hybridization because the practice of the method and its results are essentially the same whether an incomplete or complete sequence is used as a probe. For instance, a gene 513 hybridization probe is used in example 8 on p. 23 of the specification. The 31 base pair probe used in example 8 is SEQ ID NO:8, which anneals to the complement of nucleotides 866-896 of SEQ ID NO:1. A different probe that also anneals to nucleotides 36-1171 of SEQ ID

NO:1 but which also anneals to some flanking sequence, whether from the same gene or other source, would work equally well for carrying out the claimed methods and obtaining the same result. Because the presence of additional flanking sequences in addition to nucleotides 36-1171 of SEQ ID NO:1 does not change the nature of the methods or the results achievable by them, the flanking sequences of nucleotides 36-1171 of SEQ ID NO:1 are not an essential feature of the methods. Any person who performs the methods of claims 4-9 obtains the benefit of the essential features of claims 4-9 regardless of whether they add additional sequence beyond nucleotides 36-1171 of SEQ ID NO:1 onto a probe. A claim can therefore satisfy the written description requirement without specifically excluding such flanking sequences. To hold that the applicants need to disclose flanking sequences that are not essential features of the claimed methods would be an unreasonable burden and an unwarranted juxtaposition of written description standards for composition of matter claims onto method claims.

Claim 9 has been cancelled. Applicants respectfully request that the rejection of claims 4-8 as not adequately described be withdrawn.

The Examiner has rejected claims 5-8 under 35 U.S.C. § 112, first paragraph, as not enabled for detecting any allergic disease. Claims 5 and 6 have been amended to specify testing for a cedar pollen allergy. This amendment is supported by original claim 9, which has been canceled.

**35 U.S.C. § 101**

The Examiner has rejected claims 1-3 under 35 U.S.C. § 101 as directed to non-statutory subject matter. Claim 1 has been amended to specify "isolated" nucleic acids. Claims 2 and 3 have been canceled. Support for this amendment of claim 1 can be found at p.2, lines 16-26.

**35 U.S.C. § 112, Second Paragraph**

The Examiner has rejected claims 4-9 as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner has objected to the preamble of claim 4 for reciting a method for detecting a nucleic acid of claim 1 and a single method step that requires only that the method uses DNA that

hybridizes to SEQ ID NO:1. The Examiner has objected to claims 5-9 for not reciting how the purpose of the methods recited in the preamble are accomplished by completing the recited steps.

Claim 4 has been amended to include the alternative steps of hybridizing a probe or amplifying a nucleic acid molecule followed by an additional step of detecting the hybridization or amplification. This amendment is supported by lines 1-20 of page 23. This section of the specification describes both hybridizing a probe and amplifying a nucleic acid molecule to be detected using primers that anneal to gene 513 as well as detecting the hybridization and amplification products. This amendment is also supported by page 9, lines 9-14.

Claims 5 and 6 have been amended to specify that the purpose of the method, as set forth in the preamble, is accomplished by determining if the amount of gene 513 nucleic acid present in a sample from the subject is significantly higher than from a control group. These amendments are supported by page 11, lines 10-17. Claim 9 has been canceled.

The Examiner has also objected to the recitation of "a control (normal group)" in claims 5 and 6. Claims 5 and 6 have been amended to delete reference to a "normal group" and to specify that the control group has a normal level of cedar pollen specific IgE. Support for this amendment can be found at page 26, lines 13-16.

**35 U.S.C. § 102**

The Examiner has rejected claims 3 and 4 as anticipated by Baumgartner et al. This rejection is respectfully traversed as applied to the amended claims.

Baumgartner discusses a sequence (SEQ ID NO:12 of Baumgartner) that was used as a primer to amplify a gene unrelated to gene 513. This primer is identical to a primer the applicants used to amplify gene 513 because both the applicants and Baumgartner used a RACE-PCR kit sold under the trade name "Marathon cDNA Amplification Kit" from Clontech Inc. See Baumgartner at col. 17, lines 50-54. Baumgartner also refers to the AP2 primer at col. 21, line 28. See instant specification in the paragraph spanning pages 26-27. The 23 nucleotide "AP2" primer sequence is the first 23 nucleotides of SEQ ID NO:1 because SEQ ID NO:1 is the PCR product of the RACE-PCR reaction. As discussed earlier, nucleotides 24-35 of SEQ ID NO:1 correspond to the Marathon kit adaptor sequence.

Claims 1 and 4-6 have been amended to specify nucleotides 36-1171 of SEQ ID NO:1. This amendment removes the Marathon kit adaptor sequence from the scope of the claims. Claims 1 and 4-6, as amended, are not anticipated by SEQ ID NO:12 of Baumgartner. Claim 3 has been canceled. The applicants respectfully request the rejection of claim 4 be withdrawn.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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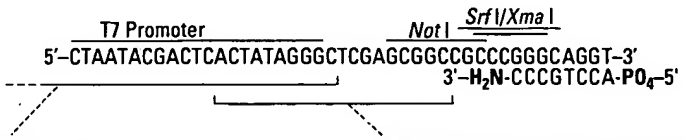
## Appendix A: Marathon cDNA Adaptor & Primers... *continued*

**Marathon cDNA Adaptor:**




**Adaptor Primer 1** (AP1; 27-mer):
5'–CCATCCTAATACGACTCACTATAGGGC–3'

**Nested Adaptor Primer 2** (AP2; 23-mer):
5'–ACTCACTATAGGGCTCGAGCGGC–3'

**Marathon cDNA Synthesis Primer** (52-mer): 5'–TTCTAGAATTCAGCGGCCGC(T)$_{30}$N$_{-1}$N–3'

*EcoR I* *Not I*

N$_{-1}$ = G, A, or C; N = G, A, C, or T
Degenerate nucleotides anchor primer at base of poly-A tail

**5'-RACE TFR Primer** (24-mer): 5'–GTCAATGTCCCAAACGTCACCAGA–3'

**3'-RACE TFR Primer** (29-mer): 5'–ATTTCGGGAATGCTGAGAAAACAGACAGA–3'

**Figure 8: Sequences of the Marathon cDNA Adaptor & Primers.** The $T_m$'s of AP1 and AP2 are 71°C and 77°C, as determined by nearest neighbor analysis (Freier *et al.*, 1986). Note, however, that only 22 of the 27 nt in AP1 bind the Adaptor during the first cycle of PCR, so the effective $T_m$ of AP1 may be actually several degrees lower. The lower effective $T_m$ of AP1 is the reason touchdown PCR works well with Marathon RACE reactions.